specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group III. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO:5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and a vector comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group IV. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO:6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group V. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID N0:7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:7, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group VI. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat

sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO:9, classifiable in class 536, subclass 24.5.

Group VII. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:4, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:4, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO:9, classifiable in class 536, subclass 24.5.

Group VIII. Claims I,7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO:9, classifiable in class 536, subclass 24.5.

Group IX. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO:9, classifiable in class 536, subclass 24.5.

Group X. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:7, wherein said polynucleotide, in the absence of inverted terminal repeat

sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO:9, classifiable in class 536, subclass 24.5.

Group XI. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XII. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo,* comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:4, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:4, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XIII. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo,* comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XIV. Claim 20, allegedly drawn to a method for expressing a protein or an

RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID N0:6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XV. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO:7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:7, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XVI. Claim 21, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO:2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO:2, wherein said fragment is at least 77 nucleotides in length and wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 536, subclass 24.1.

Office Action, pages 2-7.

Applicants provisionally elect with traverse to prosecute Group I, claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat

sequences from AAV, specifically induces expression in cardiac cells in vivo of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5. *Id.* at 2. Applicants respectfully request the reconsideration and withdrawal of the requirement for restriction between each of Groups I-X and XVI.

The Examiner acknowledges that the compositions of Groups I-X are related to each other because they are drawn to related polynucleotides. *Id.* at 4. Nevertheless, the Examiner asserts that restriction is proper because each Group "employs different molecules with different chemical properties and physical structures so that independent searches of the prior art would be required that would constitute a serious burden on the Examiner." *Id.* at 9, 10. The Examiner further asserts that a search of the polynucleotides comprising a fragment of any of SEQ ID NOs:3-7, or a fragment of a sequence that hybridizes under high stringency conditions with any of SEQ ID NOs: 3-7 in one of Groups I-V, would not encompass all of the art relevant to the polynucleotide comprising a fragment of any others of SEQ ID NOs:3-7, or a fragment of a sequence that hybridizes with any others of SEQ ID NOs: 3-7 in another of Groups I-V. *Id.* at 9. Moreover, the Examiner asserts that a search of the polynucleotide comprising a fragment of any of SEQ ID NOs:3-7, or a fragment of a sequence that hybridizes under high stringency conditions with any of SEQ ID NOs: 3-7 in Groups I-V, would not encompass all of the art relevant to the polynucleotide comprising a fragment of SEQ ID NOs:3-7, or a fragment of a sequence that hybridizes with SEQ ID NOs: 3-7, wherein said polynucleotide further comprise SEQ ID NO:9 of Groups VI-X. Finally, the

Examiner asserts that a polynucleotide comprising a fragment of SEQ ID NO: 2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO: 2, wherein said fragment is at least 77 nucleotides in length, and wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, is a polynucleotide not found in any other Group.

According to the M.P.E.P.,

> . . . each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 *et seq.* Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See *Examination of Patent Applications Containing Nucleotide Sequences,* 1192 O.G. 68 (November 19, 1996).

M.P.E.P. § 803.04.

In addition, "in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction." *Id.* Here, there are six overlapping sequences, corresponding to SEQ ID NOs:2-7. In addition, a ninth sequence, SEQ ID NO:9, is also found in the claim language.

Applicants respectfully submit that restriction between inventions classified as Groups I-X and XVI conflict with the Commissioner's decision as embodied in M.P.E.P. § 803.04. This is especially true where, as here, the Examiner requires restriction between inventions encompassing overlapping sequences derived from the same

complete sequence, the human CARP gene. Applicants submit that a search of the human CARP gene would encompass SEQ ID NOs:2-7 and that a search for the smallest fragment of the overlapping fragments claimed, would reveal all prior art related to each of SEQ ID NOs:2-7. Moreover, the sequence of the fragment of the human cardiac α-actin promoter (SEQ ID NO:9) was known prior to this application and is only part of the invention in conjunction with SEQ ID NOs:2-7. A search of the prior art for SEQ ID NOs:2-7 would also reveal if any of these CARP sequences were used in conjunction with a fragment of the human cardiac α-actin promoter. Thus, no additional searching is required. Consequently, Applicants request withdrawal of the restriction requirement between Groups I-X and XVI.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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